

Draft Guidance on Nisoldipine

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Nisoldipine

Form/Route: Extended Release Tablets/Oral

Recommended studies: 3 studies

1. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 34 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional Comments:

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2. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 17 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional comments:

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3. Type of study: Fasting
Design: Single-dose, two-way, crossover *in-vivo*
Strength: 8.5 mg
Subjects: Healthy males and nonpregnant females, general population.
Additional comments:
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Analytes to measure: Nisoldipine in plasma

Bioequivalence based on (90% CI): Nisoldipine

Waiver request of in-vivo testing: 25.5 mg based on (i) acceptable bioequivalence studies on the 34 mg strength, (ii) acceptable dissolution testing across 25.5 mg and 34 mg strengths, and (iii) proportional similarity in the formulations across 25.5 mg and 34 mg strengths.

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.fda.gov/cder/ogd/index.htm>. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each

of all strengths of the test and reference products. Specifications will be determined upon review of the application.

For modified release products, dissolution profiles generated using USP Apparatus I at 100 rpm and/or Apparatus II at 50 rpm in at least three dissolution media (pH 1.2, 4.5 and 6.8 buffer, water) should be submitted in the application. Agitation speeds may have to be increased if appropriate. It is acceptable to add a small amount of surfactant, if necessary. The following sampling times are recommended: 1, 2, and 4 hours and every 2 hours thereafter, until at least 80% of the drug is dissolved. Comparative dissolution profiles should include individual tablet data as well as the mean, range, and standard deviation at each time point for twelve tablets. Specifications will be determined upon review of the data submitted in the application.